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RETURN RECIPT REQUESTED

SANITIZED COPY

February 10, 2012

TSCA Confidential Business Information Center (7407M) EPA East – Room 6428 Attn: Section 8(e) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460-0001 Phone: (202) 564-8940

RE: 1-Butanethiol (CAS# 109-79-5) – Skin Sensitization Potential in Mice

Dear Section 8(e) Coordinator,

Chevron Phillips Chemical Company LP (CPChem) submits the attached study report in accordance with the requirements under Section 8(e) of the Toxic Substances Control Act.

This submission is not an indication that CPChem has made a determination as whether or not the chemical substance being reported may present substantial risk to health or the environment.

Both Confidential and Sanitized copies are provided. Redacting does not include chemical identity information.

You may contact me in case there are any questions.

wellen ale

Sincerely yours,

Fred Marashi



Chevron Phillips Chemical Company LP TSCA Section 8(e) Submission Confidentiality Substantiation 1-Butanethiol (syn: n-Butyl Mercaptan; CAS# 109-79-5)

1. Is your company asserting this confidential business information (CBI) claim on its own behalf? If the answer is no, please provide company name, address and telephone number of the entity asserting claim.

Yes. The study being submitted was cosponsored between Chevron Phillips Chemical Company LP (CPChem) and as part of the data generation under the European REACH program. CPChem has independently determined that the study fulfills the requirement for submission under Section 8(e) of TSCA. We do not know if the bas made the same determination and did not want to provide a submission that included the the same in error.

2. For what period do you assert your claim(s) of confidentiality? If the claim is to extend until a certain event or point in time, please indicate that event or time period. Explain why such information should remain confidential until such point.

Based on the advice from our Legal department, we would like to assert this claim indefinitely.

3. Has the information that you are claiming as confidential been disclosed to any other government agency, or to this Agency at any other time? Identify the Agency to which the information was disclosed and provide the date and circumstances of the same. Was the disclosure accompanied by a claim of confidentiality? If yes, attach a copy of said document reflection the confidentiality agreement.

This study report will be submitted as a part of our registration dossier for the substance under the European REACH program.

4. Briefly describe any physical or procedural restrictions within your company relating to the use of storage of the information you are claiming CBI.

Although the relevant health effects of the chemical substance is not kept confidential, the detail regarding process and the identities of sponsors of the study provided in the submissions made under the requirements of Section 8(e) of TSCA are considered company confidential and are not divulged except on the need to know basis and under confidentially agreement.

5. If anyone outside your company has access to any of the information claimed CBI, are they restricted by confidentiality agreement(s). If so, explain the content of the agreement(s).

Only copies of studies, but not Section 8(e) submissions may be made available to other regulatory agencies and other bodies on the need to know basis.



Chevron Phillips Chemical Company LP TSCA Section 8(e) Submission Confidentiality Substantiation 1-Butanethiol (syn: n-Butyl Mercaptan; CAS# 109-79-5)

- 6. Does the information claimed as confidential appear or is it referred to in any of the following?
 - a. Advertising or promotional material for the chemical substance or the resulting product;

No

b. Material Safety Data Sheets or other similar materials (such as technical data sheets) for the substance or resulting end product (include copies of the information as it appears when accompanying the substance and/or product at the time of transfer or sale);

No

c. Professional or trade publications; or

No

d. Any other media or publications available to the public or to your competitors.

No

7. Has EPA, another federal agency, or court make any confidentiality determination regarding information associated wit this substance? If so, provide copies of such determinations.

None

8. Describe the substantial harmful effect that would result to your competitive position if the CBI information is made available to the public. In your answer, explain the causal relationship between disclosure and any resulting substantial harmful effects. Consider in your answer such constraints as capital and marketing cost, specialized technical expertise, or unusual process and your competitors access to your customers, Address each piece of information claimed CBI separately.

The reason for claim of confidentiality is that determination that the study fits Substantial Risk criteria of Section 8(e) has been made independently by CPChem and may not be viewed as meeting the criteria by the other sponsor(s) of the study.

9. If the substance been patented in the U.S. or elsewhere? Is a patent for the substance currently pending?

Claim of confidentiality does not include chemical identity.

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Chevron Phillips Chemical Company LP TSCA Section 8(e) Submission Confidentiality Substantiation 1-Butanethiol (syn: n-Butyl Mercaptan; CAS# 109-79-5)

10. Is the substance/product commercially available and if so, for how long has it been available on the commercial market

Chemical is a commodity substance and is available on the commercial market. The following questions do not pertain to our claim of confidentiality.

- a. If on the commercial market, are your competitors aware that the substance is commercially available in the U.S.?
- b. If not already commercially available, describe what stage of research and development (R&D) the substance is in and estimate how soon and market will be established.
- c. What is the substance used for and what type of product(s)(does it appear in?
- 11. Describe whether a competitor could employ reverse engineering to identically recreate the substance?

Claim of confidentiality does not include chemical identity.

- 12. Do you assert that disclosure of this information you are claiming CBI would reveal:
 - a. Confidential processes used in manufacturing the substance;

No

b. If a mixture, the actual portions of the substance in the mixture; or

No

c. Information unrelated to the effects of the substance on human healthy or the environment?

Yes

If the answer to any of the above questions is yes, explain how such information would be revealed.

If the Section8(e) submission is make public, it will erroneously infer that the has also make the Substantial Risk determination of the study being submitted. They may not wish to have their name associated with our Section 8(e) submission in the public domain.

13. Provide the Chemical Abstract Service Registry Number for the product, if known. Is your company applying for the CAS number now or in the near future? If you have applied for a CAS number, include a copy of the contract with CAS.

Page 4 of 4



Chevron Phillips Chemical Company LP TSCA Section 8(e) Submission Confidentiality Substantiation 1-Butanethiol (syn: n-Butyl Mercaptan; CAS# 109-79-5)

The CAS# has been provided.

14. Is the substance or any information claimed CBI the subject of FIFRA regulation or reporting? If so, explain.

No



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SPONSOR

Chevron Phillips Chemical Company LP

Chevron Phillips Chemical Company LP 10001 Six Pines Dr. Suite 4103 The Woodlands, TX 77380 USA

TEST ITEM

n-BUTYL MERCAPTAN CAS No.: 109-79-5

MO NO., 103-13-0

STUDY TITLE

EVALUATION OF SKIN SENSITIZATION POTENTIAL IN MICE

USING THE LOCAL LYMPH NODE ASSAY (LLNA)

STUDY DIRECTOR

Jérémy Silvano

DATE OF ISSUE

30 December 2011

TEST FACILITY

CIT

BP 563 - 27005 Evreux - France

LABORATORY STUDY NUMBER

38206 TSS



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7.

CIT GLP certificate

SAMILIANI COPY CIT/Study No. 38206 TSS/n-BUTYL MERCAPTAN/ and Chevron Phillips Chemical Company LP

GLP COMPLIANCE STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with CIT's standard operating procedures and the following principles of Good Laboratory Practice:

OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17 and all subsequent OECD consensus documents,

Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (OJ No. L50 of 20 2 2004),

Article Annexe 2 à l'article D523-8 du code de l'environnement du 16 octobre 2007 concernant les principes de l'OCDE des Bonnes Pratiques de Laboratoire (BPL).

The solubility assay and reception of the animals for the preliminary test occurred before the signature of the final study plan by the Study Director No chemical analysis of the dosage forms was performed as part of this study. These exceptions are not considered to impact on the overall GLP status of the study.

The study was also conducted in compliance with the following Animal Health regulations, in particular:

Council Directive 86/609/EEC of 24th November 1986 on the approximation of laws, regulations and administrative provisions regarding the protection of animals used for experimental and other scientific purposes.

This study was performed at CIT, BP 563, 27005 Evreux, France.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

J. Silvano

Study completion date: 30 December Lay

Study Director

Doctor of Veterinary Medicine

d Chevron Phillips Chemical

SIGNATURE PAGE

CIT Management

J.J. Legrand

Date: 30 <u>Ne. 20 ti</u>

Director of Toxicology and Laboratory Science



Chevron Phillips Chemical

STATEMENT OF QUALITY ASSURANCE UNIT

Inspections performed at CIT

The CIT Quality Assurance Unit conducted the inspections detailed below:

	Dates				
Type of inspection	Inspection	Reported to the Study Director	Reported to Management		
Study plan	13 September 2011	13 September 2011	13 September 2011		
Amendment No. 1 to the study plan	26 September 2011	26 September 2011	26 September 2011		
Amendment No 2 to the study plan	04 October 2011	04 October 2011	04 October 2011		
Report	20 December 2011	20 December 2011	20 December 2011		

In addition, study-based inspections were carried out by the Quality Assurance Unit on similar studies performed during the same period, as detailed below:

		Dates	
Type of inspection	Inspection	Reported to the Study Director	Reported to Management
Examination	08 September 2011	08 September 2011	08 September 2011

In addition, process and facility based inspections are carried out according to the annual quality assurance program

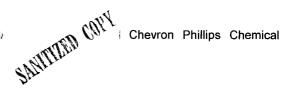
The inspections were performed in compliance with CIT Quality Assurance Unit procedures and the principles of Good Laboratory Practices.

The final report is considered to constitute an accurate and complete reflection of the study raw data.

Christelle CADIEU

CIT Quality Assurance Unit

Date. 28 December 2011



SUMMARY

The objective of this study was to evaluate the potential of the test item, n-BUTYL MERCAPTAN, to induce delayed contact hypersensitivity using the murine Local Lymph Node Assay (LLNA). Evaluation of local irritation was also carried out in parallel.

Methods

A preliminary test was first performed in order to define the concentrations of test item to be used in the main test.

In the main test, 28 female CBA/J mice were allocated to 7 groups:

- . five treated groups of four animals receiving the test item at the concentration of 5, 10, 25, 50 or 100% in Acetone/Olive Oil (AOO) (vehicle),
- . one negative control group of four animals receiving the vehicle,
- . one positive control group of four animals receiving the positive control item, α-hexylcinnamaldehyde (HCA), a moderate sensitizer, at the concentration of 25% in a mixture acetone/olive oil (4/1; v/v).

During the induction phase, the test item, vehicle or positive control item was applied over the ears (25 µL per ear) for 3 consecutive days (days 1, 2 and 3). After 2 days of resting, the proliferation of lymphocytes in the lymph node draining the application site was measured by incorporation of tritiated methyl thymidine (day 6). The obtained values were used to calculate Stimulation Indices (SI).

The irritant potential of the test item was assessed in parallel by measurement of ear thickness on days 1, 2, 3 and 6.

Results

Clinical signs and mortality

No unscheduled deaths occurred and no clinical signs were observed during the preliminary or main test.

Local irritation

At the concentration of 100% of the test item, 4/4 females presented dryness of the skin on day 6 and 1/4 showed an erythema on day 6 and 4/4 females showed increase in ear thickness (i.e. 15.15% between day 6 and day 1).

No other local reactions or notable increase in ear thickness were observed in the other study animals.

Proliferation assay

The acceptance criterion was met; this experiment was therefore considered valid.

The results are presented in the following table:

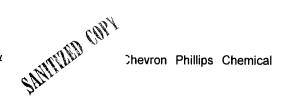
Treatment	Concentration (%)	Irritation level	Stimulation Index (SI)
Test item	5	non-irritant	0.67
Test item	10	non-irritant	0.43
Test item	25	non-irritant	2.45
Test item	50	non-irritant	5.38
Test item	100	slightly irritant	14.40
HCA	25	-	3.97

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The threshold positive value of 3 for the SI was exceeded in the positive control group (SI = 3.97) and at the concentrations of 50 and 100% of the test item. The EC₃ value (theoretical concentration resulting in a SI value of 3) was 30%.

Conclusion

Under the experimental conditions of this study, the test item, n-BUTYL MERCAPTAN, induced delayed contact hypersensitivity in the murine Local Lymph Node Assay.



1. INTRODUCTION

1.1 OBJECTIVE

The objective of this study was to evaluate the potential of the test item, n-BUTYL MERCAPTAN, to induce contact hypersensitivity, using the murine Local Lymph Node Assay (LLNA).

This study was based on the design adopted by ICCVAM (Interagency Coordination Committee on the Validation of Alternative Methods, ICCVAM 1999) and ECETOC (Monograph No. 29 Skin sensitization Testing for the Purpose of Hazard Identification and Risk Assessment, September 2000), with the addition of the evaluation of local irritation.

1.2 REGULATORY COMPLIANCE

The study was based on the following guidelines:

- OECD Guideline for Testing of Chemicals No. 429 "Skin Sensitisation: Local Lymph Node Assay", 24th April 2002,
- Commission Regulation (EC) No. 440/2008, B.42, 30 May 2008.

1.3 IN-HOUSE ETHICS REVIEW PROCEDURE

CIT has an in-house ethics review procedure, which covers animal welfare within the facility. The activities of the ethical committee, which are not within the scope of the Good Laboratory Practice regulations, were reviewed as part of the AAALAC accreditation procedure and the FELASA recommendations.

The CIT Ethical Committee (CEC) reviews all the study plans, in order to ensure that:

- . animal use is carefully considered and fully justified.
- . all possibilities for reduction, refinement and replacement have been evaluated,
- . every effort is made to achieve a high standard of animal welfare.

The study plan was submitted for ethical review before the initiation of the study.

During the study, the CEC was regularly informed of:

- any amendments to the study plan which could have had an impact on animal welfare,
- any clinical findings or unexpected situations which could have led to animal stress or discomfort.

Any decisions or requests were made after consultation with a veterinarian, or after taking expert advice, and were reported to the Study Director.

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2. MATERIALS AND METHODS

2.1 TEST AND CONTROL ITEMS

2.1.1 Identification

2.1.1.1 Test item

Supplier : CHEVRON PHILLIPS CHEMICALS

. Name : n-BUTYL MERCAPTAN

CAS number : 109-79-5
Batch number : 11GPNBM03
Expiry date : July 2012
Description : clear liquid
Purity/Composition : 99.2%

Container : one brown glass flaskDate of receipt : 22 August 2011

Storage conditions : keep tightly closed in a dry and well-ventilated place, room temperature and

protected from light (see § Study plan adherence).

An analysis certificate, provided by the Sponsor, is presented in Appendix 1.

All remaining test item will be destroyed 6 months after the last use.

2.1.1.2 Positive control

. Supplier : Aldrich

. Name : α-hexylcinnamaldehyde (HCA)

Other name : alpha-hexylcinnamaldehyde.tech.85%

Both names correspond to the same test item.

. Batch number : MKAA2596

. Expiry date : 17 February 2012 . Description : yellow liquid

Purity : 95.9%

. Container : one brown glass flask
. Date of receipt : 17 February 2011

. Storage conditions : at room temperature and protected from light.

An analysis certificate, provided by the Supplier, is presented in Appendix 1.

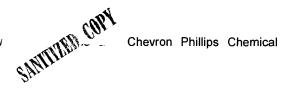
2.1.1.3 Vehicle

The vehicle used for the positive control was a mixture of Acetone/Olive Oil (4/1, v/v) (AOO):

- . Acetone: batch No. 0001428703, supplied by Merck,
- . Olive Oil: batch No. K41254613, supplied by Sigma.

A solution was obtained at the concentration of 50% in AOO.

As the test item is a liquid that can be sampled using a pipette, the maximum achievable concentration was 100%.



2.1.2 Dosage form preparation

The test item was administered as a solution in the vehicle. The test item was mixed by vortex with the required quantity of vehicle.

The test item concentrations were expressed in % (v/v).

The positive control was prepared at the concentration of 25% (v/v) a mixture of Acetone/Olive Oil (4/1; v/v) (AOO).

Dosage forms preparations were prepared by the CIT Pharmacy extemporaneously on the day of each administration.

The dosage forms were stored at room temperature and delivered to the study room in stoppered plastic tubes.

2.1.3 Reagent used for the proliferation assay

The reagent used for the proliferation assay was [³H] methyl-thymidine (³H-TdR), batch No. 201109, supplied by PerkinElmer (Courtaboeuf, France).

Three days before the injections, the required quantity of 3 H-TdR was diluted in 0.9% NaCl, batch No. 1A043, supplied by Lavoisier (20 μ Ci in 250 μ L of 0.9% NaCl per animal). The obtained solution was stored at +4°C and protected from light.

2.2 TEST SYSTEM

2.2.1 Animals

Number:

- . preliminary test: 4 nulliparous and non pregnant females,
- . main test: 28 nulliparous and non pregnant females.

Species and sanitary status: CBA/J mice.

Reason for selection of species: this inbred strain was chosen on the basis of previous studies performed in our laboratory, in which CBA/J mice showed the best proliferative response. Females have been chosen since this sex is recommended by the International Guidelines.

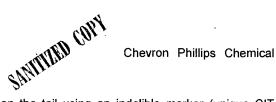
Breeder: Janvier, Le Genest-Saint-Isle, France.

Age/weight: on the beginning of the treatment period, the animals of the preliminary and main tests were approximately 8 weeks old. In the main test, they had a mean body weight of 20.8 g (range: 19.6 g to 22.4 g).

Receipt: upon arrival at CIT, the animals were given a clinical examination to ensure that they are in good condition.

Allocation to groups: upon arrival at CIT, the animals were allocated to the groups (by sex) using a manual randomization procedure. A larger number of animals than necessary was acclimated to permit the selection and/or replacement of individuals.

Acclimation: the animals were acclimated to the study conditions 13 days (preliminary test) or 11 days (main test) before the beginning of the treatment period. At the end of acclimation period, the required number of animals was selected according to clinical condition and body weight.



Identification: the animals were individually identified on the tail using an indelible marker (unique CIT identity number).

2.2.2 Environmental conditions

From arrival at CIT, the animals were housed in a barriered rodent unit.

The animal room conditions were set as follows:

temperature : 22

: 22 ± 2°C,

. relative humidity : 50 ± 20%,

. 50 ± 20 /0,

light/dark cycle

: 12 h/12 h (7:00 - 19:00),

ventilation

: approximately 12 cycles/hour of filtered, non-recycled air.

The corresponding instrumentation and equipment are checked and calibrated at regular intervals. The temperature and relative humidity are recorded continuously and the records checked daily and filed.

2.2.3 Housing

The animals were housed by group of two (preliminary test) or four (main test) in polycarbonate cages (Techniplast 1145T, 435 cm 2 , 36.9 x 15.6 x 13.2 cm) containing autoclaved sawdust (SICSA, Alfortville, France).

Each cage contained two enrichments (mouse hut and cocoon) with possibility of rotation during the study. In the main test, on day 6 before the ³H-TdR injections, the animals were individually housed in disposable crystal polystyrene cages (22.0 cm x 8.5 cm x 8.0 cm).

2.2.4 Food and water

All animals had free access to SSNIFF R/M-H pelleted maintenance diet, batch No. 9615507, (SSNIFF Spezialdiäten GmbH, Soest, Germany) and tap water (filtered using a 0.22 micron filter) contained in bottles. The diet formula is presented in Appendix 2.

2.2.5 Contaminant analyses

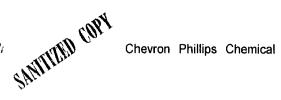
The batches of diet and sawdust were analyzed by the suppliers for composition and contaminant levels. Bacterial and chemical analyses of water are performed regularly by external laboratories. These analyses include the detection of possible contaminants (pesticides and heavy metals). No contaminants that could have interfered with or prejudiced the outcome of the study were found in the diet, drinking water or sawdust.

2.3 TREATMENT

2.3.1 Rational for concentration selection

The maximum concentration tested in the main test was selected according to the criteria specified in the OECD Guidelines and on the basis of the data that were obtained in the preliminary test:

- . the vehicle should be selected on the basis of producing a homogeneous preparation suitable for application of the test item,
- the concentrations were selected from the concentration series 100% (when test item can be sampled by a pipette), 50%, 25%, 10%, 5%, 2.5%, 1%, 0.5%, etc.,
- the maximum concentration of the test item was selected to avoid overt systemic toxicity and excessive local skin irritation the latter being defined by an > 25% increase of the ear thickness.



2.3.2 Preliminary test

2.3.2.1 Treatment groups

To assess the irritant potential of the test item (through ear thickness measurement), a preliminary test was performed in four animals.

The treatment groups for the preliminary test are detailed in the following table:

Group	Number of	Concentration (%)		
	animals	Left ear	Right ear	
1	2 females	10	25	
2	2 females	50	100	

2.3.2.2 Application

On days 1, 2 and 3, a dose-volume of 25 μ L of the appropriate dosage form preparation was applied to the dorsal surface of both ears (one concentration per ear), using an adjustable pipette fitted with a plastic tip. In order to avoid licking, to ensure an optimized application of the test materials and to facilitate ear thickness measurement, the animals were placed under light isoflurane anesthesia during the administration.

No massage was performed but the tip was used to spread the preparation over the application site. No rinsing was performed.

2.3.3 Main test

2.3.3.1 Treatment groups

The treatment groups for the main test are detailed in the following table:

Group	Number of animals	Treatment	Concentration (%)
3	4 females	Vehicle	0
4	4 females	Test item	5
5	4 females	Test item	10
6	4 females	Test item	25
7	4 females	Test item	50
8	4 females	Test item	100
9	4 females	Positive control item	25% of HCA

2.3.3.2 Application

On days 1, 2 and 3, a dose-volume of 25 µL of the control or dosage form preparations was applied to the dorsal surface of both ears, using an adjustable pipette fitted with a plastic tip.

In order to avoid licking and to ensure an optimized application of the test materials, the animals were placed under light isoflurane anesthesia during the administration.

No massage was performed but the tip was used to spread the preparation over the application site. No rinsing was performed.



2.4 CLINICAL EXAMINATIONS

2.4.1 Morbidity and mortality

Each animal was checked for mortality and morbidity once a day during the acclimation, treatment and observation periods, including weekends and public holidays.

2.4.2 Clinical signs

Each animal was observed once a day, at approximately the same time, for the recording of clinical signs.

2.4.3 Body weight

The body weight of each animal was recorded once during the acclimation period, and then on the first day of treatment and on the day of sacrifice.

2.4.4 Ear thickness measurements and recording of local reactions

Ear thickness measurements and recording of local reactions were performed in order to assess any possible irritant effect of the test item, as potent irritants may yield positive lymphoproliferative responses of equivocal significance in the LLNA.

On days 1, 2 and 3 (before each cutaneous application) and on day 6 (immediately after sacrifice), the thickness of both ears of each preliminary test animal (groups 1 and 2) and the left ear of each main test animal (groups 3 to 8) was measured, using a micrometer.

No measurement of ear thickness was performed for the main test animals of the positive control group (group 9).

The irritation level of the test item was determined according to the following table:

% increase in ear thickness between day 1 and day 6	Irritation level	Interpretation
< 10%	l	Non-irritant
≥10 - < 25%	II	Slightly irritant
≥ 25%	III	Irritant

Any local reaction was also recorded (coloration of the skin, erythema, crusts...).

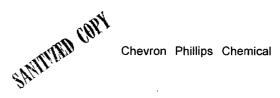
2.5 AURICULAR LYMPH NODE CELL (ALNC) PROLIFERATION ASSAY

2.5.1 Intravenous injection of ³H-TdR and sampling of auricular lymph nodes

Lymph node cell proliferative response was measured as described by Kimber and Dearman (1). On day 6 of the main test, all animals of all groups received a single intravenous injection of 250 µL of 0.9% NaCl containing 20 µCi of ³H-TdR (specific activity of 20 Ci/mmol) *via* the tail vein.

Approximately 5 hours later, the main test animals were sacrificed by an intraperitoneal injection of pentobarbital sodium followed by a cervical dislocation and the auricular lymph nodes were excised. The lymph nodes were pooled for each experimental group. A single cell suspension of ALNC was prepared by mechanical disaggregation in Petri dishes with the plunger of a syringe.

⁽¹⁾ Kimber, I. and Dearman, R.J. (1991) Investigation of lymph node cell proliferation as a possible immunological correlate of contact sensitizing potential. Food. Chem. Toxicol: 29, 125-129.



2.5.2 Preparation of auricular lymph node cell suspensions and determination of proliferation

Cell suspensions were washed once with 15 mL of 0.9% NaCl. Each cell suspension was then centrifuged and pellets were precipitated with 3 mL of 5% (w/v) trichloroacetic (TCA) at +4°C overnight. After a last centrifugation, the pellets were precipitated with 1 mL of 5% TCA. Three millilitres of Ultima Gold^{xR} scintillation fluid (Packard) were added in order to measure incorporation of 3 H-TdR using β -scintillation counting.

The results were expressed as disintegrations per minute (dpm) per group and as dpm/node.

Stimulation Indices (SI) were calculated according to the following formula:

2.5.3 Acceptance criteria

The study is considered valid if the SI for the positive control is higher than the threshold positive value of 3.

2.5.4 Evaluation of results

The test item is considered as a skin sensitizer when the SI for a dose group is ≥ 3 together with consideration of a dose-response relationship. Other relevant criteria such as radioactivity levels and ear thickness are also taken into account to evaluate the data.

The EC_3 value (theoretical concentration resulting in a SI value of 3) was determined by linear interpolation of points on the dose-response curve, immediately above and below the 3-fold threshold. The equation used for calculation of EC_3 was:

$$EC_3 = c + [(3 - d)/(b-d)] \times (a - c)$$

where a = the lowest concentration giving stimulation index > 3; b = the actual stimulation index caused by a; c = the highest concentration failing to produce a stimulation index of 3; and d = the actual stimulation index caused by c.

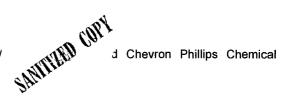
Categorization of contact allergens on the basis of relative skin sensitization potency, using EC₃ values derived from the LLNA (1)

EC ₃ value	Category
< 0.1%	extreme sensitizer
≥ 0.1 - < 1%	strong sensitizer
≥ 1 - < 10%	moderate sensitizer
≥ 10 - ≤ 100%	weak sensitizer

2.6 PATHOLOGY: fate of the animals

On completion of the observation period, all animals were sacrificed by an intraperitoneal injection of pentobarbital sodium followed by a cervical dislocation.

⁽¹⁾ Kimber I. et al. (2003); Food and Chemical Toxicology 41: 1799-1809.



2.7 ARCHIVING

The following study materials are retained in the archives of CIT (BP 563, 27005 Evreux, France) for 10 years after the draft report has been sent:

- study plan and amendments,
- . raw data,
- . correspondence,
- final report and any amendments.

The total duration of archiving (depending on regulations) will be the responsibility of the Sponsor.

2.8 CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

Procedure	Date		
Study plan approved by:			
. Study Director	19 September 2011		
. Study Monitor	03 October 2011		
Solubility assay	13 September 2011		
Preliminary test			
Experimental starting date			
(day of arrival of the animals)	15 September 2011		
First day of the treatment	28 September 2011		
Main test			
Day of arrival of the animals	22 September 2011		
First day of the treatment	05 October 2011		
End of the <i>in vivo</i> phase			
(day of necropsy of the last animal)	10 October 2011		
Experimental completion date	11 October 2011		

2.9 STUDY PLAN ADHERENCE

The study was performed in accordance with study plan No. 38206 TSS and subsequent amendments, with the following deviation from the agreed study plan:

the test item was kept protected from light in excess.

This deviation was considered not to have compromised the validity or integrity of the study.

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3. RESULTS

3.1 PRELIMINARY TEST

3.1.1 Mortality (Appendix 3.1)

No unscheduled deaths occurred during the preliminary test.

3.1.2 Clinical signs (Appendix 3.1)

No clinical signs were observed in any animals.

3.1.3 Ear thickness measurements and local reactions (Appendices 4 and 5.1)

No local reactions were noted in any animals.

No notable increase in ear thickness was observed in group 2 animals (treated at the concentration of 100%).

The highest concentration retained for the main test was therefore 100%.

3.1.4 Body weight (Appendix 6.1)

The body weight of group 2 animals was unaffected by the test item-treatment.

3.2 MAIN TEST

3.2.1 Mortality (Appendix 3.2)

No unscheduled deaths occurred during the main test.

3.2.2 Clinical signs (Appendix 3.2)

No clinical signs were observed in any animals.

3.2.3 Ear thickness measurements and local reactions (Appendices 4 and 5.2)

In group 8 (treated at the concentration of 100%), 4/4 females presented dryness of the skin on day 6 and 1/4 showed an erythema on day 6.

No other local reactions were observed in animals.

In group 8 (treated at the concentration of 100%), 4/4 females showed increase in ear thickness (i.e. 15.15% between day 6 and day 1). However, the increase in ear thickness remained within the limit of 25% established in the guideline. No other notable increase in ear thickness was observed.

3.2.4 Body weight (Appendix 6.2)

The body weight change of test item-treated animals was similar to that of control animals.

3.2.5 Proliferation assay (Table 1)

The threshold positive value of 3 for the SI was exceeded in the positive control group (SI = 3.97). The experiment was therefore considered valid. In groups 7 and 8 (corresponding to the concentrations of 50 and 100%), the threshold positive value of 3 for the SI was also exceeded. The EC₃ value (theoretical concentration resulting in a SI value of 3) was 30%.

4. CONCLUSION

Under the experimental conditions of this study, the test item, n-BUTYL MERCAPTAN, induced delayed contact hypersensitivity in the murine Local Lymph Node Assay.

TABLE

CIT/Study No. 38206 TSS/n-BUTYL MERCAPTAN/
Company LP

and Chevron Phillips Chemical

Table 1. Proliferation assay (mean values)

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and Chevron Phillips Chemical

Table 1

Group	Treatment and concentrations	Number of nodes per group	dpm per group	dpm per node	Stimulation index (SI)	Increase in ear thickness (% between day 1 and day 6)	Irritation level	EC ₃ value
3	Vehicle	8	3227	403.38		11.34		
4	Test item 5%	8	2149	268.63	0.67	5.05	I	
5	Test item 10%	8	1398	174 75	0 43	5.26	I	,
6	Test item 25%	8	7910	988.75	2.45	5.10	I	30%
7	Test item 50%	8	17354	2169 25	5.38	6.32	I	
8	Test item 100%	8	46481	5810.13	14.40	15.15	П	
9	HCA 25%	8	12822	1602.75	3.97			

NA = not applicable

dpm = disintegrations per minute

I = non-irritant (increase in ear thickness < 10%)

II = slightly irritant (increase in ear thickness > 10 - <25%) EC₃ value = theoretical concentration resulting in a SI value of 3

stimulation index =

dpm of treated group dpm of control group

CIT/Study No. 38206 TSS/n-BUTYL MERCAPTAN/. and Chevron Phillips Chemical Company LP

APPENDICES

Chevron Phillips Chemical

1. Test item and reference item analysis certificates



CoA Date: 08/09/2011

Certificate of Analysis

Shipped To: CHEVRON PHILLIPS CHEMICALS

VLSB Magazijn Jules Servaes 1

KRUISWEG 2

ANTWERPEN 01 2040

Recipient: AERTS

Fax:

PO #: 4503117156 CPC Delivery #: 88310123 Ship Date: 08/11/2011 Package/Mode: 2 OZ BTL Quantity: 1 EA

Certification Date: 07/30/2011

Transportation ID:

Shelf Life: Undetermined

Product: N-BUTYL MERCAPTAN TECH, 2 OZ BTL

Material Code:1021486

Lot Number: 11GPNBM03

Property	Test Method	Specification	Value	Unit
Appearance	Visual	Clear with no parti	Clear with no par	rti
Cloud Point	ASTM D-2386 mod	<= -20	< -20	FAH
Distillation - IBP	ASTM D-1078	> ≖ 96	98	CEL
Distillation - DP	ASTM D-1078	<= 110	100	CEL
n-Butyl Mercaptan	Chromatography	>= 98,5	99,2	WT%
Di-N-Butyl Disulfide	Chromatography	<= 0,3	0,0	WT*

The data set forth herein have been carefully compiled by Chevron Phillips Chemical Company LP. However, there is no warranty of any kind, either expressed or implied, applicable to its use, and the user assumes all risk and liability in connection therewith.

KE Inkutt

Ken Inkrott

Quality, Applications and Technical Service Manager

For CoA questions contact Kim Lindley at 806-275-5577

Page 1 of 1

Certificate of Analysis

Product Name

α-Hexylcinnamaldehyde,

technical grade, 85%

Product Number Product Brand

291285 ALDRICH

CAS Number Molecular Formula 101-86-0 $C_6H_5CH=C[(CH_2)_5CH_3]CHO$

216.32

Molecular Weight

SPECIFICATION

LOT MKAA2596 RESULTS

Appearance (Color) Appearance (Form) Yellow to Yellow-Green

Yellow

Infrared spectrum

Liquid Conforms to Structure Liquid Conforms

Purity (GC) Specification Date: Date of QC Release: ≥84.0 %

95.9 % JAN 2009 FEB 2009

Print Date:

FEB 09 2009

Barbara Rajzer, Supervisor

Quality Control

Milwaukee, Wisconsin USA

// and Chevron Phillips Chemical

2. Diet formula



SsniffR/M-H

Complete diet for rats/mice - maintenance

•			
		Constituents	
Crude proteins	19.00 %	Calcium	1.00 %
Crude fat	3.30 %	Phosphorus	0.70 %
Crude fiber	4.90 %	Sodium	0.25 %
Crude ash	6.70 %	Magnesium	0.20 %
		Potassium	0.90 %
Amino Acids		Vitamins (je kg)	
Lysine	1.00 %	Α	15,000 IE
Methionine	0.30 %	D3	1,000 iE
Cystine	0.30 %	E	100 mg
Glycine	0.90 %	B1	10 mg
Leucine	1.30 %	B2	20 mg
Isoleucine	0.70 %	B6	12 mg
Arginine	1.20 %	B12	80 µg
Phenylalanine	0.90 %	Biotin	400 µg
Tryptophan	0.25 %	Pantothenic acid	30 mg
Histidine	0.50 %	Choline	1,600 mg
Tyrosine	0.60 %	Folic acid	4 mg
Aspartic acid	1.70 %	Nicotic acid	60 mg
Glutaminic acid	3.80 %	K3	5 mg
Valine	0.90 %	Inositol	50 mg
Threonine	0.70 %		
Trace elements (je kg)		ME (je kg)	12.2 MJ
Manganese	90 mg		
Copper	12 mg		
Zinc	75 mg	Item numbers	
lodine	2 mg	V1530 Meal	
Iron	220 mg	V1531 Micromeal	
Selenium	0.2 mg	V1534 Pellets 10 r	mm
Cobalt	2 mg	V1535 Pellets 15 r	mm

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3. Clinical signs: individual findings

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3.1 Preliminary test



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CLINICAL HISTORY - INDIVIDUAL FINDINGS PRELIMINARY TEST

Study No.:

38206 TSS

Sex:

Female

Group:

1

Period:

Days -13 to 6

Animal No.	Clinical history	
301	No clinical signs	From days -13 to 6
	Final sacrifice	Day 6
302	No clinical signs	From days -13 to 6
	Final sacrifice	Day 6

Sex:

Female

Group:

2

Period:

Days -13 to 6

Animal No.	Clinical history	
303	No clinical signs	From days -13 to 6
	Final sacrifice	Day 6
304	No clinical signs	From days -13 to 6
	Final sacrifice	Day 6

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3.2 Main test

COLL Chevron Phillips Chemical

CLINICAL HISTORY - INDIVIDUAL FINDINGS MAIN TEST

Study No.:

38206 TSS

Dosage form : Vehicle
Sex: Female

Sex: Female
Period: Days -11 to 6

Animal No.	Clinical history	
01	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
02	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
03	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
04	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6

Dosage form : Test item at 5%

Sex: Female
Period: Days -11 to 6

Animal No.	Clinical history	
05	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
06	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
07	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
08	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6

Dosage form : Test item at 10%

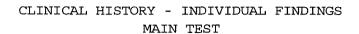
Sex: Female Period: Days -11 to 6

Animal No.	Clinical history	
09	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
10	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
11	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
12	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6

Dosage form : Test item at 25%

Sex: Female
Period: Days -11 to 6

Animal No.	Clinical history	
13	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
14	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
15	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
16	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6



SANTHIAN COPY

Study No.:

38206 TSS

Dosage form : Test item at 50%

Sex:

Female

Period:

Days -11 to 6

Animal No.	Clinical history	
17	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
18	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
19	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
20	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6

Dosage form : Test item at 100%

Sex: Period: Female

remare Days -11 to 6

Animal No.	Clinical history	
21	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
22	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
23	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
24	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6

Dosage form : HCA at 25%

Sex:

Period:

Female Days -11 to 6

Animal No.	Clinical history	
25	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
26	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
27	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6
28	No clinical signs	From days -11 to 6
	Final sacrifice	Day 6

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4. Dermal examinations: individual findings

LOCAL REACTIONS

Cuarra	Dosage form	A ! 1	Days					
Group		Animal – No.	1	2	3	6		
3	vehicle	01	0	0	0	0		
		02	0	0	0	0		
		03	0	0	0	0		
		04	0	0	0	0		
4	test item	05	0	0	0	0		
	5%	06	0	0	0	0		
		07	0	0	0	0		
		08	0	0	0	0		
5	test item	09	0	0	0	0		
	10%	10	0	0	0	0		
		11	0	0	0	0		
		12	0	0	0	0		
6	test item	13	0	0	0	0		
J	25%	14	0	Ŏ	0	0		
		15	0	0	0	0		
		16	0	0	0	0		
7	test item	17	0	0	0	0		
•	50%	18	0	0	0	0		
		19	0	0	0	0		
		20	0	0	0	0		
8	test item	21	0	0	0	S		
•	100%	22	0	0	0	S		
		23	0	o	o	S		
		24	0	0	0	E/S		

^{0 =} no cutaneous reaction

S = dryness of the skin

E = erythema

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5. Ear thickness measurements: individual values

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5.1 Preliminary test

EAR THICKNESS MEASUREMENT (mm) AND LOCAL REACTIONS

				D	1	D	2	D	3		D6	
Group Animal No	Concentration		Ear	Local	Ear	Local	Ear	Local	Ear	Local	%	
стопр	Aninai No	%		Thickness	reaction	Thickness	reaction	Thickness	reaction	Thickness	reaction	
	301	10	LE	0 27	0	0 27	0	0.26	0	0 26	0	-3 70
1		25	RE	0.26	0	0 26	0	0.30	0	0 26	0 ,	0.00
1	302	10	LE	0.26	0	0 26	0	0.25	0	0.25	0	-3 85
		25	RE	0.26	0	0.27	0	0.26	0	0 27	0	3.85
	303	50	LE	0.25	0	0.25	0	0.25	0	0.26	0	4 00
2	1	100	RE	0.25	0	0.28	0	0.26	0	0 29	0	16.00
2	304	50	LE	0.24	0	0 24	0	0 25	0	0.25	0	4 17
	304	100	RE	0.25	0	0.27	Q	0.27	0	0 30	0	20.00

RE = right ear LE = left ear

D = day

0 =no cutaneous reaction

[%] = percentage of ear thickness increase compared to day 1

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5.2 Main test

EAR THICKNESS MEASUREMENT (mm)

_	_					Days			
Group	Dosage form	Animal [*] No.	1	2	d1	3	d2	6	d3
3	vehicle	01	0.25	0.26	0.01	0.26	0.01	0.27	0.02
5	Venicie	02	0.22	0.24	0.02	0.25	0.03	0.25	0.03
		03	0.25	0.26	0.01	0.25	0.00	0.29	0.04
		04	0.25	0.26	0.01	0.26	0.01	0.27	0.02
		M	0.24	0.26	0.01	0.26	0.01	0.27	0.03
		SD	0.02	0.01	0.00	0.01	0.01	0.02	0.01
		% (*)			5.15		5.15		11.34
4	test item	05	0.25	0.26	0.01	0.27	0.02	0.27	0.02
	5%	06	0.24	0.24	0.00	0.26	0.02	0.26	0.02
		07	0.25	0.26	0.01	0.26	0.01	0.26	0.01
		08	0.25	0.26	0.01	0.25	0.00	0.25	0.00
		M	0.25	0.26	0.01	0.26	0.01	0.26	0.01
		SD	0.01	0.01	0.01	0.01	0.01	0.01	0.01
		% (*)			3.03		5.05		5.05
_									
5	test item	09	0.23	0.24	0.01	0.25	0.02	0.24	0.01
	10%	10	0.24	0.25	0.01	0.24	0.00	0.25	0.01
		11 12	0.24	0.25	0.01	0.25	0.01	0.25	0.01
		14	0.24	0.25	0.01	0.26	0.02	0.26	0.02
		M	0.24	0.25	0.01	0.25	0.01	0.25	0.01
		SD	0.00	0.01	0.00	0.01	0.01	0.01	0.01
		% (*)			4.21		5.26		5.26
		% (*)			4.21		5.26		5

M = mean

SD = standard deviation

^{(*) =} percentage of ear thickness increase compared to day 1

d1 = difference of ear thickness between day 2 and day 1

d2 = difference of ear thickness between day 3 and day 1

d3 = difference of ear thickness between day 6 and day 1



EAR THICKNESS MEASUREMENT (mm)

			Days							
Group	Dosage form	Animal No.	1	2	dl	3	d2	6	d3	
6	test item	13	0.25	0.25	0.00	0.25	0.00	0.26	0.01	
J	25%	14	0.24	0.26	0.02	0.25	0.01	0.25	0.01	
		15	0.25	0.26	0.01	0.25	0.00	0.25	0.00	
		16	0.24	0.24	0.00	0.25	0.01	0.27	0.03	
		M	0.25	0.25	0.01	0.25	0.01	0.26	0.01	
		SD	0.01	0.01	0.01	0.00	0.01	0.01	0.01	
		% (*)			3.06		2.04		5.10	
			^^*	0.05	0.00	0.24				
7	test item	17	0.25	0.25	0.00	0.26	0.01	0.26	0.01	
	50%	18	0.23	0.25	0.02	0.26	0.03	0.26	0.03	
		19 20	0.22 0.25	0.23 0.25	0.01	0.23	0.01	0.23	0.01	
		20	0.23	0.23	0.00	0.20	0.01	0.26	0.01	
		M	0.24	0.25	0.01	0.25	0.02	0.25	0.02	
		SD	0.02	0.01	0.01	0.02	0.01	0.02	0.01	
		% (*)			3.16		6.32		6.32	
		21	0.25	0.27	0.02	0.27	0.02	0.21	0.06	
8	test item 100%	21	0.25	0.27	0.02	0.27	0.02	0.31	0.06	
	10070	22 23	0.25 0.25	0.27 0.26	0.02	0.28 0.26	0.03	0.28 0.27	0.03	
		23 24	0.23	0.20	0.01	0.25	0.01	0.27	0.02	
					0.03		0.01			
		M	0.25	0.27	0.02	0.27	0.02	0.29	0.04	
		SD	0.01	0.01	0.01	0.01	0.01	0.02	0.02	
		% (*)			8.08		7.07		15.15	

M = mean

SD = standard deviation

^{(*) =} percentage of ear thickness increase compared to day 1

d1 = difference of ear thickness between day 2 and day 1

d2 = difference of ear thickness between day 3 and day 1

d3 = difference of ear thickness between day 6 and day 1

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6. Body weight and body weight change: individual values

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Chevron Phillips Chemical

6.1 Preliminary test

BODY WEIGHT AND BODY WEIGHT CHANGE (g) $\mathsf{PRELIMINARY} \ \mathsf{TEST}$

Group	Animal No.	-3	1	6	1/6
1	301	19.6	19.7	19.6	-0.1
1	302	19.0	20.0	20.0	0.0
	M	19.4	19.9	19.8	0.0
	SD	0.4	0.2	0.3	0.1
2	303	21.2	20.6	21.0	0.4
	304	20.4	19.1	20.2	1.1
	M	20.8	19.9	20.6	0.7
	SD	0.6	1.1	0.6	0.5

M = mean

SD = standard deviation

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Chevron Phillips Chemical

6.2 Main test



BODY WEIGHT AND BODY WEIGHT CHANGE (g) MAIN TEST

			Days				
Group	Dosage form	Animal No	-3	l l	6	1/6	
3	vehicle	01	19.4	20 5	19 9	-0.6	
-	vemore	02	21 1	22 0	21 1	-0.9	
		03	19.6	20 7	196	-1 1	
		04	20.4	21.3	198	-1 5	
		M	20 1	21 1	20 1	-10	
		SD	0 8	0 7	0.7	0 4	
		05	20 1	20 6	10.7	-09	
4	test item	05			19 7		
	5%	06	20.2	20 9	190	-19	
		07	21 5	22.4	21 0	-1 4	
		08	19 1	20 1	19 5	-0.6	
		M	20 2	21 0	198	-12	
		SD	1.0	10	09	06	
			40 -				
5	test item	09	19 9	20 2	18 8	-1 4	
	10%	10	20 3	21 0	20.2	-0 8	
		11	210	20 9	19.7	-1 2	
		12	18 9	20.2	19 4	-0.8	
		M	20.0	20 6	19 5	-1.1	
		SD	09	0 4	0.6	0 3	
							
6	test item	13	21 3	21 2	20 5	-0 7	
	25%	14	20 0	21 8	19.9	-19	
		15	20 9	21 5	20 9	-0 6	
		16	198	20.4	20 2	-0.2	
		М	20 5	21.2	20.4	-0 9	
		SD	0 7	0 6	0 4	0 7	
							
7	test item	17	20 5	21.7	198	-19	
	50%	18	20 2	20 2	196	-0.6	
		19	199	20 3	19 7	-0 6	
		20	19 0	19 9	18 1	-1 8	
		M	199	20 5	19 3	-12	
		SD	06	0 8	0 8	0 7	
8	test item	21	198	198	198	0.0	
	100%	22	19 5	20 5	20 8	03	
		23	196	19 9	19.7	-0 2	
		24	19.5	21 1	20 7	-0 4	
		М	196	20.3	20.3	-0.1	
		SD	0 1	06	0 6	03	
9	HCA	25	20 7	19 6	20 6	10	
	25%	26	19 7	21 7	19 3	-2 4	
		27	22 3	21 8	216	-0 2	
		28	197	20 0	18 8	-1 2	
		M	20 6	20 8	20 1	-0 7	

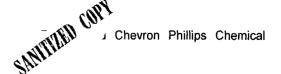
M = mean SD = standard deviation

CIT/Study No. 38206 TSS/n-BUTYL MERCAPTAN/. Company LP

Chevron Phillips Chemical

7. CIT GLP certificate

CIT/Study No. 38206 TSS/n-BUTYL MERCAPTAN/ Company LP





GROUPE INTERMINISTERIEL DES PRODUITS CHIMIQUES

CERTIFICAT DE CONFORMITE AUX BONNES PRATIQUES DE LABORATOIRE SELON LES DIRECTIVES 2004/9/CE ET 2004/10/CE

CERTIFICATE OF COMPLIANCE WITH GOOD LABORATORY PRATICES ACCORDING TO DIRECTIVES 2004/9/CE AND 2004/10/CE

Certificat no: 2011/40

Société ou organisme :

IFM RECHERCHE - CENTRE INTERNATIONAL DE TOXICOLOGIE (CIT)

Company:

MISEREY - BP 563 - 27005 EVREUX CEDEX

Installation d'essais :

Test facilities :

IFM RECHERCHE - CENTRE INTERNATIONAL DE TOXICOLOGIE (CIT)

MISEREY - BP 563 - 27005 EVREUX CEDEX

Vu les articles D.523-8 et suivants du code de l'environnement relatifs au groupe interministériel des produits chimiques,

Having regard to the articles D.523-8 and onwards relating to the interministerial group of chemical products (GIPC).

Vu les résultats de l'inspection périodique réalisée par le Comité français

d'accréditation (COFRAC) - Section Laboratoires - le :

17 et 18 mars 2011

Having regard to the results of the periodic inspection realised by the French 17 and 18 March 2011

Committee of accreditation (COFRAC) - Laboratory Section - on the :

Vu l'avis du GIPC en date du :

23 juin 2011

Having regard to the GIPC's opinion dated.

23 June 2011

La conformité aux principes des BPL de l'installation précitée est reconnue dans les domaines suivants : Compliance with the principles of GLP is recognized for the facility above in the following areas:

- 2 études de toxicité (toxicity testing)
- 3 études de mutagénicité (mutagenicity testing)
- 4 études écotoxicologiques sur les organismes aquatiques et terrestres (Environmental toxicity studies on aquatic or terrestrial organisms)
- 8 méthodes de chimie analytique et cliniques (y compris métabolisme) (analytical and clinical chemistry testing)

Fait à Paris, le 19 juillet 2011

Le Président,

Jean-Pierre FALQUE-PIARROTIA

Secrétariat général du GIPC - DGCIS, Service de l'industrie, bureau de la chunie - 12, rue Villiot - 75572 Paris cedex 12 Téléphone : 01 53 44 96 ±0 - Télécopie : 01 53 44 91 72

> MINISTERE DE L'ECONOMIE DES FINANCES ET DE L'INDUSTRIE